

Birch Pollen-Related Food Hypersensitivity: Influence of Total and Specific IgE Levels

A Multicenter Study*

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Total IgE, RAST results with tree pollen allergens, and prick test results with birch, grass and mugwort pollen allergens were correlated to 872 hay fever patients' reported food hypersensitivity (FH). A positive correlation was found between FH and the RAST and prick test results with birch pollen allergen. At each level of birch pollen sensitivity the incidence of FH was lower in patients with high total IgE than in those with lower total IgE. A negative correlation was found between grass pollen allergy and FH in birch pollen allergics. It is suggested that antigens in some foods have a specific ability to bridge anti-birch IgE molecules on mast cells. An explanation of the negative correlation between FH and total IgE and grass pollen allergy could be that a high number of non-birch-specific IgE molecules on the mast cells will reduce the probability that two anti-birch IgE molecules should bind on nearby sites.

Key words: birch pollen; food hypersensitivity; hay fever; immunoglobulin E; radioallergosorbent test.

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A correlation exists between birch pollen allergy and hypersensitivity to some fruits, roots and nuts (5, 7, 10, 11). A quantitative relationship has been established; the more pronounced the sensitivity to birch pollen, the higher is the incidence of food hypersensitivity (FH) (7, 9). The mechanism responsible for this interrelationship is not clear. Some studies indicate that cross-reacting allergens could be the explanation (3, 12). In another study no partial identity could be demonstrated between birch

pollen allergen and extracts from some birch pollen-related foodstuffs (2). The possibility that lectins could be responsible for the birch pollen-associated FH has been proposed (2, 13). Lectins are proteins present in some vegetable foods which are able to bind to specific oligosaccharide configurations on glycoproteins, including the carbohydrate side chain of IgE.

In the present study hay fever patients' reported FH was correlated to their total IgE and

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specific IgE antibody concentrations against tree pollen allergens and skin prick test (SPT) results with various pollen allergens.

MATERIAL AND METHODS

Patients

This investigation is a part of a multicenter study regarding tree pollen allergy. Sixteen centers took part in the study comprising 872 hay fever patients, 464 males and 408 females with a mean age of 27 (range 8–67) years. The mean duration of their hay fever was 11 years (range 1–49).

In vivo tests

Skin tests were performed as prick tests (SPT) on the forearm or on the back. Reactions were read after 10–20 min and graded according to the recommendations of the Standardization Committee of the Northern Society of Allergy (1). Thus a wheal of the same size as that of positive histamine reference was recorded as 3+ and each additional plus indicated an approximate doubling of the reaction.

In vitro tests

For the determinations of specific IgE antibody concentrations the Radioallergosorbent Test (RAST) was used in accordance with the manufacturer's recommendations (Phadebas RAST®, Pharmacia Diagnostics AB, Uppsala, Sweden). Results were expressed in Phadebas RAST classes 0–4. Total IgE levels were determined using the Phadebas IgE PRIST®, (Pharmacia Diagnostics AB, Uppsala, Sweden) according to the instructions for use of the test procedure.

Allergens

Specific IgE antibodies were determined against different tree pollens (birch, alder, hazel, beech, elm, maple and willow). For SPT a Neohelisen 500 PNU/ml glycerinated birch pollen allergen extract batch No. 56577 was employed (Allergopharma, Reinbek, GFR). Various grass and mugwort pollen extracts were used at those clinics cooperating in the study (extracts from

Allergologisk Laboratorium, Copenhagen, Denmark; Dome/Hollister-Stier, Slough, England; Allergopharma, Reinbek, GFR; or Allergy Laboratory, Sahlgren's Hospital, Göteborg, Sweden).

Food hypersensitivity (FH)

Patients were questioned whether they had noticed hypersensitivity symptoms when eating or handling various birch pollen-related foodstuffs (nuts, apple, pear, plum, cherry, peach, potato peel etc.) (7). The answers were recorded as "yes", "no", or "I don't know".

Statistics

Pitman's non-parametric correlation test (6) and the chi-square test were used for the statistical calculations. When the relationship between FH and total IgE was analyzed, the background variable, birch pollen allergy, was taken into account by using the following non-parametric partial correlation test: the patients were divided into subgroups according to strength of their SPT with birch pollen allergen. Within each subgroup Pitman's test variable (6) was calculated. The results from the different groups were then pooled to a summarizing test (13).

RESULTS

A history of FH was given by 482 of the 872 patients. A strong positive correlation ($P < 0.001$) was found between FH and SPT results with birch pollen allergen (Table 1) and between FH and RAST results with birch (Fig. 1), as well as with alder and oak pollens ($P < 0.001$).

When RAST results from all eight tree pollen allergens used were added up and related to the occurrence of FH a positive correlation was found ($P < 0.001$). All patients with RAST class score of 26 or more were found food hypersensitive. No correlation was found between FH and the SPT results with grass pollen or with mugwort pollen. Among birch pollen allergic patients, on the other hand, a

Table 1
Food hypersensitivity in relation to prick test results with *birch pollen* allergen

	Prick test results, birch (No. plusses) ^a								
	0	1	2	3	4	5	6	7	8
Number of patients	141	32	50	174	212	175	63	15	10
Incidence of food hypersensitivity (%) ^b	21	28	22	56	69	71	70	80	90

^a For definition of plusses, see Methods.

^b Significance of positive correlation between prick test results and food hypersensitivity: $P < 0.001$.

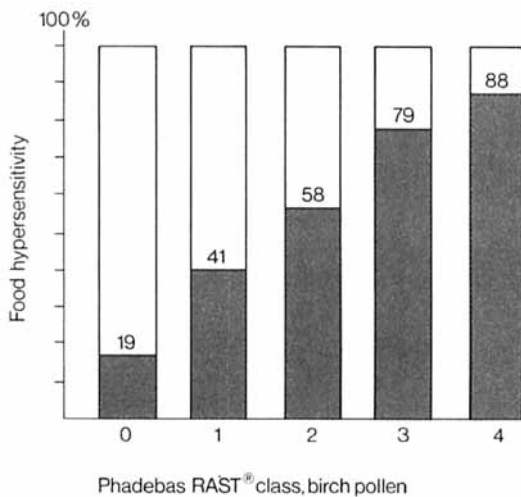


Fig. 1. Relationship between RAST class with birch pollen allergen and incidence of food hypersensitivity. Figures indicate percentages.

Table 2

Food hypersensitivity in relation to prick test results with *grass pollen* allergen in birch pollen allergic patients (prick test reaction $\geq 1+$ with birch pollen allergen)

	Prick test results, grass pollen		
	Negative	Doubtful (1–2+)	Positive ($\geq 3+$)
Number of patients	184	71	434
Incidence of food hypersensitivity (%) ^a	70	69	57

^a Significance of negative correlation between prick test results and food hypersensitivity: $P < 0.001$.

Table 3

Relationship between food hypersensitivity, total IgE and prick test results with birch pollen allergen

Total IgE kU/l	Incidence of food hypersensitivity (%) ^a Prick test results, birch				Sign. ^b
	0	1–2+	3+	$\geq 4+$	
< 100	18 (50)	38 (24)	69 (54)	72 (127)	***
100–499	23 (31)	13 (23)	50 (56)	69 (137)	***
≥ 500	33 (3)	17 (6)	48 (23)	58 (58)	NS

^a Figures in brackets indicate number of patients from which percentages have been calculated.

^b Statistical significance of the positive correlation between food hypersensitivity and prick test results, according to Pitman's test.

*** $P < 0.001$. NS = not significant.

Table 4

Relationship between food hypersensitivity, total IgE and RAST results with birch pollen allergen

Total IgE kU/l	Incidence of food hypersensitivity (%) ^a RAST class, birch				Sign. ^b
	0	1	2	3–4	
< 100	21 (106)	70 (10)	79 (53)	88 (86)	***
100–499	16 (73)	23 (13)	36 (45)	87 (115)	***
> 500	20 (10)	33 (9)	43 (7)	64 (64)	**

^a Figures in brackets indicate number of patients from which percentages have been calculated.

^b Statistical significance of the positive correlation between food hypersensitivity and RAST results, according to Pitman's test.

** $P < 0.01$. *** $P < 0.001$.

negative correlation was found between FH and SPT reactions with grass pollen (Table 2).

A close correlation between total IgE and specific IgE antibody concentrations in birch pollen allergic patients could be demonstrated ($P < 0.001$).

Patients with allergy against both grass and tree pollens had higher total IgE (318 ± 19 kU/l) than patients with tree pollen allergy only (254 ± 23 kU/l) ($P < 0.001$).

Patients with FH had lower total IgE (247 ± 18 kU/l) than patients without FH (314 ± 26 kU/l) ($P < 0.05$). In birch pollen allergics with a total IgE < 100 kU/l the incidence of FH was 68% and in those with a total IgE ≥ 100 kU/l it was 58% ($P < 0.01$).

In order further to evaluate the relationship between FH and total IgE and birch pollen allergy we divided the patients into three groups: IgE < 100 kU/l, IgE 100–500 kU/l and IgE > 500 kU/l. In each of these groups the incidence of FH was related to the SPT and RAST results with birch pollen allergen. The results are shown in Tables 3 and 4. At each level of birch pollen sensitivity the incidence of FH was higher among patients with low total IgE than among patients with higher total IgE.

When the relationship between FH and total IgE was analyzed with a statistical method taking into account the degree of birch pollen sensitivity (see Methods), a significant negative correlation was found ($P < 0.01$).

DISCUSSION

The connection between tree pollen allergy and hypersensitivity to nuts and fruits has been recognized in Sweden for many years. This knowledge is of importance in allergy diagnosis in Scandinavia: itching in the mouth, elicited by nuts and fruits in patients with springtime hay fever is an indirect proof of birch pollen allergy (9). In other parts of Europe, e.g. England, where birch pollen allergy is of very limited clinical importance, this "para-birch phenomenon" has a lesser diagnostic significance (Frankland, personal communication).

The mechanism behind the birch pollen-associated FH is not wholly understood. Efforts

to demonstrate cross-reactivity and allergen identity between tree pollen and various food-stuffs have given contradictory results (2, 3, 4). Some studies strongly suggest that the birch-related FH is a reagin-mediated, type I, allergy. Lahti et al. (12) coupled apple seed proteins to paper discs and showed an IgE specific uptake with serum from apple sensitive individuals. Dreborg & Fouchard (5) showed that apple, carrot, potato and hazelnut reactivity was transferable in Prausnitz-Küstner test. Other studies have suggested that lectins in fruits could be the mediators of FH in tree pollen allergic patients (12, 13).

Lectins are supposed to elicit histamine release from mast cells by binding to the carbohydrate-rich Fc-part of the IgE molecule. This binding is not allergen specific and should be as frequent between all kinds of IgE antibodies. Apparently this can not explain the fact that FH occurs mostly among birch pollen allergics.

In this study we have shown a strong correlation between birch pollen allergy and FH: the stronger the skin test or RAST result with birch pollen, the higher the frequency of FH. This finding is in accordance with earlier studies (5, 7, 9). An unexpected finding was, however, that the frequency of FH among birch pollen allergics was lower if their total IgE level was high. In birch pollen allergics there was also a negative correlation between FH and skin test reactions to grass pollen, indicating that the risk for reaction to fruits among these patients is smaller if they are simultaneously sensitized to grass. Similar results were obtained in an earlier study (9).

We have no definite explanation of the negative correlation between FH and total IgE and grass pollen allergy. The findings fit, however, with the hypothesis that the birch-associated FH is caused by cross-reacting allergens in foods, when they cross-link two adjacent mast cell-bound birch pollen-specific IgE molecules. The chances for this reaction to take place should be highest in cases of strong monovalent birch pollen allergy. If, on the other hand, there are numerous non-birch specific IgE molecules, e.g. anti-grass pollen reagins on the mast cells, the probability of food antigens

binding two anti-birch IgE molecules on nearby sites is smaller. The chance of allergens cross-reacting with birch pollen to elicit a mast cell degranulation should thus be lower.

This could explain why the frequency of FH decreases in cases of simultaneous grass pollen allergy or in cases with high total IgE for other reasons.

In the Nordic countries birch is widespread and sensitization to birch pollen is a common cause of springtime hay fever (8). The probability of a monovalent allergy to birch pollen is relatively high in comparison with other parts of Europe where birch is not so dominant. This could explain why the phenomenon of birch-associated FH is mainly a Nordic observation.

Our results strongly indicate that antigens in some foods have a specific ability to bridge anti-birch IgE molecules on mast cells. The conclusion is based on a statistical analysis of symptoms and test results in a clinical patient material. More basic immunological work is needed to give the ultimate proof that cross-reacting allergens are the basis for the birch pollen-associated hypersensitivity to nuts, fruits and roots.

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